AMENDMENTS TO THE CLAIMS

1.   (Currently amended) A copolymer composition that functionally binds to a major histocompatibility complex (MHC) protein HLA-DQ comprising semi-random sequence copolymers having a length of at least about 30 amino acid residues with at least two fixed anchor residues which are separated by 7 amino acid residues, wherein:

(1) the anchor residue is selected from aspartic acid residue (D) and glutamic acid residue (E);

(2) the remainder of the copolymer has a random sequence comprising at least two amino acid residues, one amino acid selected from each amino acid residue group

(a) alanine (A) or glycine (G); and

(b) leucine (L), isoleucine (I), valine (V), methionine (M), threonine (T), serine (S), and cysteine (C);

optionally further comprising proline (P).

2. - 4. (Canceled)

5.   (Currently amended) A copolymer composition comprising amino acid residues:

(1) aspartic acid, alanine, leucine, and glutamic acid (DALE);

(2) aspartic acid, alanine, isoleucine, and glutamic acid (DAIE);

(3) aspartic acid, alanine, valine, and glutamic acid (DAVE); or

(4) aspartic acid, alanine, threonine, and glutamic acid (DATE);

(5) aspartic acid, alanine, serine, glutamic acid (DASE);

(6) aspartic acid, glycine, leucine, and glutamic acid (DGLE);

(7) aspartic acid, glycine, isoleucine, and glutamic acid (DGIE);

(8) aspartic acid, glycine, valine, and glutamic acid (DGVE);

(9) aspartic acid, glycine, threonine, and glutamic acid (DGTE); or

(10) aspartic acid, glycine, serine, glutamic acid (DGSE)

in a random sequence.

6.   (Canceled)

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7.   (Currently amended) The copolymer composition of claim 3 or 4 5, wherein the molar

output ratio of amino acid residues D:A:X:E or D:G:X:E, wherein X is L, I, V, S, or T, is

about:

(1) 1:10:3:1;

(2) 1:15:3:1;

(3) 1:25:15:5; or

(4) 1:3:1.5:0.2;

wherein the variability in the molar output ratios comprises a range of about 10% between the different

amino acids.

8.   (Canceled)

9.   (Currently amended) The copolymer composition of claim 3 or 4 5, wherein the molar input

ratio of amino acid residues D:A:X:E or D:G:X:E, wherein X is L, I, V, S, or T, is about:

(1) 1:5:3:1;

(2) 1:25:15:5; or

(3) 1:1:1.5:0.2.

10.-17. (Canceled)

18.   (Currently amended) The copolymer composition of claim 13 1, wherein the HLA-DQ is

associated with an autoimmune disease selected from pre-diabetes, diabetes mellitus, celiac

disease, unwanted immune response, and allergy.

19.-22. (Cancelled)

23.   (Currently amended) The copolymer composition of claim 13 1, wherein the HLA-DQ is

HLA-DQ2 (a combination of alleles DQA1*0501-DQB1*0201) or HLA-DQ8 (a

combination of alleles DQA1*03-DQB1*0302).

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24.   (Original) A pharmaceutical composition for treatment of an autoimmune disease, comprising a pharmaceutically effective amount of a copolymer composition comprising copolymers that functionally bind to an HLA-DQ molecule associated with the autoimmune disease, and a pharmaceutically acceptable carrier and/or an excipient.

25.   (Currently amended) The pharmaceutical composition of claim 24, wherein the copolymer composition is the copolymer composition ~~of claim 18~~ functionally binds to a major histocompatibility complex (MHC) protein HLA-DQ comprising semi-random sequence copolymers having a length of at least about 30 amino acid residues with at least two fixed anchor residues which are separated by 7 amino acid residues, wherein:

    (1) the anchor residue is selected from aspartic acid residue (D) and glutamic acid residue (E);
    (2) the remainder of the copolymer has a random sequence comprising at least two amino acid residues, one amino acid selected from each amino acid residue group
    (a) alanine (A) or glycine (G); and
    (b) leucine (L), isoleucine (I), valine (V), methionine (M), threonine (T), serine (S), and cysteine (C);

    optionally further comprising proline (P); and

    wherein the HLA-DQ is associated with an autoimmune disease selected from pre-diabetes, diabetes mellitus, celiac disease, unwanted immune response, and allergy.

26.   (Original) The pharmaceutical composition of claim 25, further comprising an additional therapeutically active agent.

27.-30. (Canceled)

31.   (Currently amended) The pharmaceutical composition of claim 26, wherein the additional therapeutically active agent is insulin or an immunosuppresant.

32.-39. (Cancelled)

40.   (Original) A method for treating an autoimmune disease comprising administering to a subject having the autoimmune disease a therapeutically effective amount of a copolymer composition that comprises one or more random sequence copolymers that binds to an HLA-DQ molecule associated with the autoimmune disease.

41.   (Currently amended) The method of claim 40, wherein said copolymer composition is a copolymer composition of claim 18 functionally binds to a major histocompatibility complex (MHC) protein HLA-DQ comprising semi-random sequence copolymers having a length of at least about 30 amino acid residues with at least two fixed anchor residues which are separated by 7 amino acid residues, wherein:

      (1) the anchor residue is selected from aspartic acid residue (D) and glutamic acid residue (E);

      (2) the remainder of the copolymer has a random sequence comprising at least two amino acid residues, one amino acid selected from each amino acid residue group

(a) alanine (A) or glycine (G); and

(b) leucine (L), isoleucine (I), valine (V), methionine (M), threonine (T), serine (S), and cysteine (C);

optionally further comprising proline (P); and

wherein the HLA-DQ is associated with an autoimmune disease selected from pre-diabetes, diabetes mellitus, celiac disease, unwanted immune response, and allergy..

42.   (Original) The method of claim 41, further comprising administering a second therapeutically active agent.

43.-46. (Canceled)

47.   (Currently amended) The method according to claim 46 40, wherein the diabetic condition autoimmune disease is selected from: pre-diabetes, insulin-dependent diabetes mellitus (type I), and type II diabetes celiac disease, unwanted immune response, and allergy.

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48.-67. (Canceled)

68.   (Currently amended) A method for prophylactically treating a subject at risk of <u>or having</u> <u>pre-conditions for</u> developing an autoimmune disease <u>selected from prediabetes, diabetes</u> <u>mellitus, celiac disease, unwanted immune disease, and allergy</u>, comprising administering the copolymer of claim 18, wherein the onset of the autoimmune disease is delayed or prevented.

69.-73. (Canceled)

74.   (Currently amended) The method according to claim ~~73~~<u>68</u>, wherein the subject or <u>one or</u> <u>more genetically related</u> family members of the subject have high blood glucose or high auto-antibody levels, compared to a control subject that does not have the condition.

75.   (Currently amended) ~~A~~ <u>The</u> method <u>according to claim 68, wherein the</u> ~~of treating a~~ subject <u>is a</u> recipient of pancreatic islet transplantation, ~~the method comprising administering to the subject~~ ~~a composition according to any of claims 1-18 and 25-33.~~

76.-82. (Canceled)

83.   (Original) A method for identifying a copolymer that is therapeutically effective to treat an HLA-DQ mediated autoimmune disease comprising:

      (a) synthesizing a random copolymer of amino acids selected from:

          (1) hydrophobic, aliphatic residues (leucine, isoleucine, valine, methionine)

          (2) acidic residues (aspartic acid, glutamic acid)

          (3) small hydrophilic residues (serine, cysteine, threonine)

          (4) small aliphatic residues (alanine, glycine)

          and

          (5) proline.

      (b) determining binding of said copolymer to an HLA-DQ molecule;

      (c) comparing binding of said copolymer to said HLA-DQ molecule with binding of a known autoantigenic peptide to said HLA-DQ;

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(d) selecting said copolymer which binds to said HLA-DQ molecule substantially more strongly than said known autoantigenic peptide; and

(e) determining activation of T-helper cells moderated by said HLA-DQ molecule presenting said copolymer.

84.   (Original) The method of claim 83, wherein said autoantigenic peptide is selected from:

(1) a peptide comprising amino acid residues 9-23 of human insulin;

(2) a peptide comprising amino acid residues 206-220 of human GAD; and

(3) a peptide comprising amino acid residues 441-460 of human HSP60.

85.   (Original) The method of claim 84, wherein said HLA-DQ molecule is selected from DQA1*03-DQB1*0302, DQA1*0501-DQB1*0201, a trans dimer between HLA-DQA1*0501-DQB1*0201 and HLA-DQA1*03-DQB1*0302, DQA1*03/B1*0302, DQB1*0201/DQA1*0501, DQB1 *0201 and DQA1*03.

86.   (Original) The method of ~~any of~~ claims 83 ~~to 85~~, wherein the copolymer <u>modified for detection, said modification selected from</u> ~~is biotinylated~~ <u>biotinylation and labeling with FITC</u>.

87.-96. (Cancelled)